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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/821,389

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Terrance P. Snutch

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MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER

PACKARD, BENJAMIN J

ART UNIT

PAPER NUMBER

1612

MAIL DATE

DELIVERY MODE

01/07/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/821,389	Applicant(s) SNUTCH ET AL.	
	Examiner Benjamin Packard	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2008 and 22 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7, 9-16 and 19-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 9-15, 19-28 and 30 is/are rejected.
- 7) ☒ Claim(s) 16, 29 and 31 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

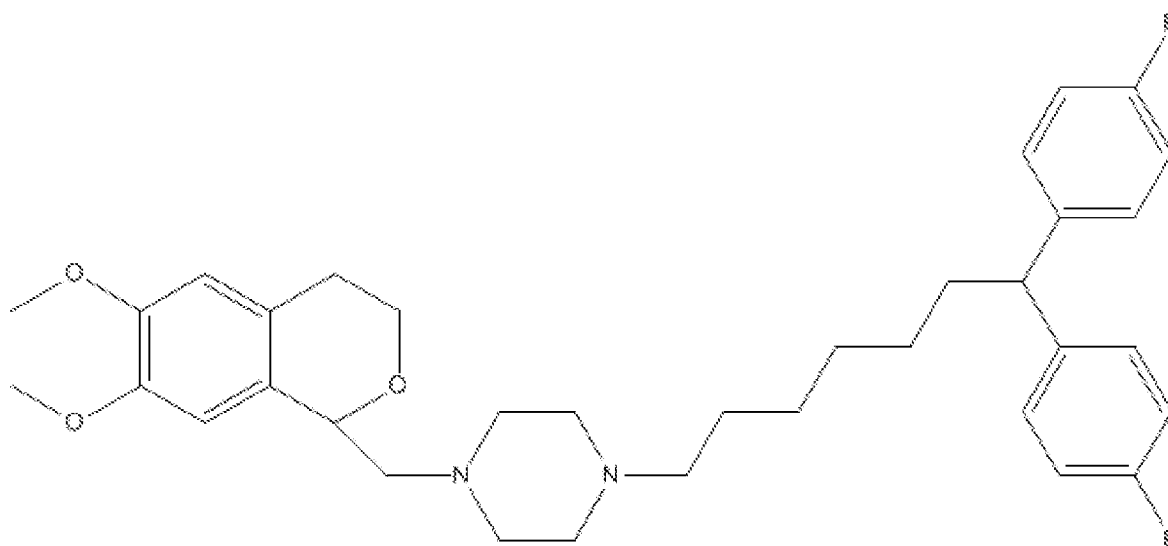
- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed 06/23/2008, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Species Election Expanded

Note, because the elected species could not be found, the prior art search was broadened to a non-elected species. The species selected by the examiner for further consideration was:



1-(7,7-bis(4-fluorophenyl)heptyl)-4-((6,7-dimethoxyisochroman-1-yl)methyl)piperazine

Claim Rejections - 35 USC § 112 – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 9-15, 19-28, and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The first paragraph of 35 USC 112 requires that the specification contain a written description of *the invention*. Accordingly, where a particular compound has not been *specifically* named or mentioned in any manner, one is left to select from mere *possibilities* encompassed by the broad disclosure, with no guide indicating or directing that this particular selection should be made rather than any of the many others which could also be made. In re Ruschig, 154 USPQ 118, 122 (CCPA 1967). As elaborated by the court:

Specific claims to single compounds require reasonably specific supporting disclosure and while we agree with the appellants, as the board did, that *naming* is not essential, something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required. Surely, given time, a chemist could name (especially with the aid of a computer) all of the half million compounds within the scope of the broadest claim, which claim is supported by the broad disclosure. This does not constitute support for each compound individually when separately claimed.

Here, claims 1 and 19 use the phrase “fused aromatic or heteroaromatic systems” as possible substituents Ar and the phrase “non-interfering (non-hydrogen)

Art Unit: 1612

substituents” for substituents Ar and/or R1-R3. Such terms are extremely broad insofar as a fused system appears to include an extremely large class of substituents where the ring system is not defined and non-interfering substituents may also be an extremely large class of substituents. Note, the specification does define some non-interfering substituents at paragraph 38 and some fused bicyclic and tricyclic ring systems at paragraph 35 and compounds P3, P35, etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 9-15, 19-28, and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the bicyclic and tricyclic ring systems and non-interfering substituents discussed above (see paragraph 38 and some fused bicyclic and tricyclic ring systems at paragraph 35 and compounds P3, P35, etc), does not reasonably provide enablement for synthesis with the broader “fused aromatic or heteroaromatic systems” and “non-interfering (non-hydrogen) substituents”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

1) The breadth of the claims: The instant claims are directed to a large number of compounds, with considerably different substituents attached thereto. Thus, the breadth of the claim is very large.

2) The nature of the invention: The invention is a chemical compound used as a pharmaceutical.

3) The state of the prior art: The state of the prior art is that the drugs and the receptor react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses a hydrogen changes the properties altogether. A good example is a theophylline verses caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no reasonable predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way, such changing Ar and/or R1-R3. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Also the state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the pharmacological activity required for instant claim 1. There is no reasonable predictability and no established correlation between in vitro activity and the treatment of diseases as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent

Art Unit: 1612

one of ordinary skill in the art from accepting any compound as a pharmaceutical composition on its face.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: Even when similar starting material are used under the same conditions the products obtained are different.

As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) " Dorwald F. A. Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

Thus synthesis of these compounds is unpredictable.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. Only limited substituents on the compounds at Ar and/or R1-R3 are disclosed. The availability of the starting material that is needed to prepare the invention as claimed is also at issue here. As per MPEP

Art Unit: 1612

2164.01 (b): A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in In re Ghiron, 442 F.2d 985,991,169 USPQ 723,727 (CCPA 1971), made clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. In re Howarth, 654 F.2d 103, 105,210 USPQ 689, 691 (CCPA 1981). There are no starting materials provided with respect to the various substituents.

7) The existence of working examples: The instant specification has a limited number of examples with respect to the various Ar and/or R1-R3 substituents as discussed above. The state of the art indicates that even when the reactants are similar, and the reaction conditions are the same, it is not necessary that it would form the same products.

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably synthesized as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the claimed invention in its “full

Art Unit: 1612

scope” a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

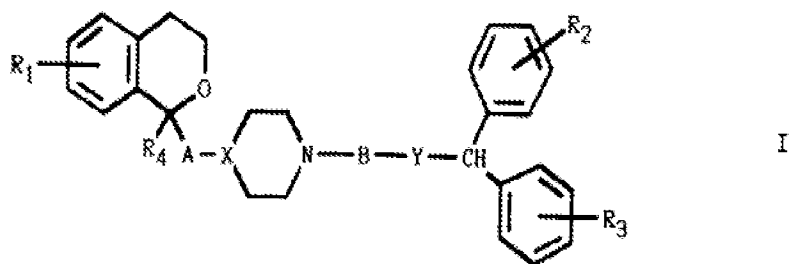
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Claims 1-5, 7, 9-15, 19-28, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laigle (EP 0458387, see IDS dated 2/19/08).

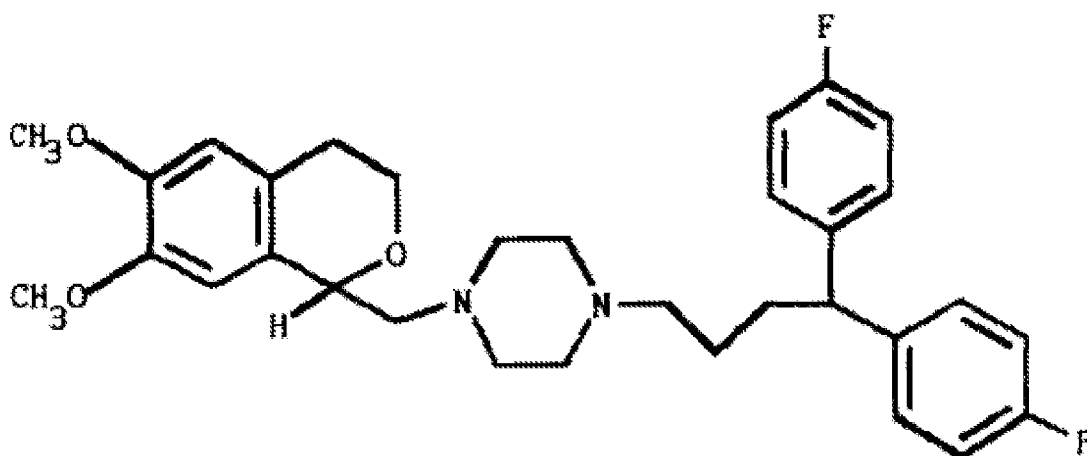
Laigle discloses in claim 1 the class of compounds of :

Art Unit: 1612



where B and Y may be a 1-6 carbon chain when Y is a bond or B is 2-6 carbons chain when Y is a group selected from O, S, or NR₅.

The closest preferred embodiment is disclosed in claim 5:



It differs from the instantly claimed class of compounds insofar as B and Y are together only 3-member chains.

It would be obvious to one of ordinary skill in the art, when looking to the general formula disclosed, to modify the preferred embodiment by extending B to be a six member carbon chain as suggested in the disclosure of the general class. Note, the fused-ring system appears to read on the instant definition of AR, where Ar may be a six-membered ring which is a fused aromatic system.

Status of claims

Claims 16, 29, and 31 are objected to as being dependent upon a rejected base claim, but appear to be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-R 8-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1612

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612